

PATENT COOPERATION TREATY

NMS
SLRFrom the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

WRITTEN OPINION

(PCT Rule 66)

To:

NOONAN, William
KLARQUIST, SPARKMAN, CAMPBELL,
LEIGH & WHINSTON, LLP
One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
ETATS-UNIS D'AMERIQUEDate of mailing
(day/month/year) 07.08.2001Applicant's or agent's file reference
4239-55779**REPLY DUE** within 2 month(s)
from the above date of mailingInternational application No.
PCT/US00/23736International filing date (day/month/year)
29/08/2000Priority date (day/month/year)
30/08/1999International Patent Classification (IPC) or both national classification and IPC
C12Q1/68

DOCKETED FOR: 10/7/01

Applicant

THE GOVERNMENT OF THE UNITED STATES ...

COMPUTER ☒
CARD ☒
BOOK ☒
BKPR ☒
ANN. SVE ☒

1. This written opinion is the first drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain document cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.**Also:** For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 30/12/2001.

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner

Heirero, M

Formalities officer (incl. extension of time limits)

Digiusto, M

Telephone No. +49 89 2399 8162



I. Basis of the opinion

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-32 as originally filed

Claims, No.:

1-45 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	
Inventive step (IS)	Claims	37-44 (part)
Industrial applicability (IA)	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

SECTION V

2. CITATIONS AND EXPLANATIONS

- 2.1 Except for the subject-matter objected to in item 2.2 below (i.e. Claims 37-44, in part) present Claims 1-45 would appear to relate to subject-matter which is novel and non-obvious over the available prior art, as required by Art. 33(2) and (3) PCT. Claims 1-45 also appear to satisfy the requirements of Art. 33(4) PCT.
- 2.2 Under their present wording not all the devices (apparatus) for sequencing a nucleic acid molecule encompassed by independent Claims 37 and 44 comprise, as an essential structural component, a polymerase which includes a donor fluorophore. In particular, in those embodiments encompassed (i) by Claim 37, in which the entity attached to the subject substrate is either an oligonucleotide primer or a sample nucleic acid, and (ii) by Claim 44, in which the entity attached to the glass microscope slide is either an oligonucleotide primer or a sample nucleic acid, a polymerase including a donor fluorophore does not necessarily form part of the claimed devices.

However, the aforementioned devices according to Claims 37 and 44, which do not contain a polymerase including a donor fluorophore as essential constitutive element of the device, would *per se* not be suitable to solve the technical problem of the present invention. As a consequence no inventive contribution over the related prior art would appear to be involved in the provision of such devices, contrary to the requirements of Art. 33(3) PCT.

The same objection (Art. 33(3) PCT) affects *mutatis mutandis* the subject-matter encompassed by dependent Claims 38-43 insofar as a polymerase including a donor fluorophore does not necessarily form part of the corresponding devices therein claimed.

- 2.3 The applicant is requested to file new claims which take account of the above comments (and of the comments in Section VIII).

Concerning a possible reformulation of independent Claims 37 and 44, attention is drawn to the fact that, a definition of a device (i.e. an apparatus) by its use or for a certain method would render the said claim unclear, contrary to Art. 6 PCT (cf PCT Guidelines, C-III, 4.8 and especially 4.8a).

- 2.4 The applicant is requested to file amendments by way of replacement pages in the manner stipulated by Rule 66.8(a) PCT. In particular, fair copies of the amendments should be filed preferably in triplicate.

Moreover, the applicant's attention is drawn to the fact that, as a consequence of Rule 66.8(a) PCT the examiner is not permitted to carry out any amendments under the PCT procedure, however minor these may be.

- 2.5 In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT).

If the applicant regards it as appropriate these indications could be submitted in handwritten form on a copy of the relevant parts of the application as filed.

- 2.6 Any information the applicant may wish to submit concerning the subject-matter of the invention, for example further details of its advantages or of the problem it solves, and for which there is no basis in the application as filed, should be confined to the letter of reply rather than be incorporated into the application, Article 34(2)(b) PCT.

SECTION VII

1. If the Applicants are aware of registered trade marks used in the description (e.g. "Triton" or "Tween", see pages 20, 23 and 24) they should identify them as such.

2. The expression "hereby/herein incorporated by reference" in respect of prior art documents (cf page 10, line 8; page 11, line 23; page 12, lines 9-10, 13 and 38; page 12, line 7; page 18, line 37; page 19, line 7; page 20, lines 3, 19-20, 25-26 and 39; page 22, lines 19 and 22; page 23, line 38; page 24, lines 12, 15 and 18; page 25, line 32; page 26, line 1; page 27, line 9 and page 29, lines 24-25) leads to a doubt as to whether the requirements of the description being self-contained are satisfied (see PCT Guidelines C-II, 4-17).

SECTION VIII

1. It is clear from the description as a whole that the presence of a polymerase carrying a donor fluorophore (e.g. a GFP-polymerase) is a feature essential to the performance of the invention.

Since independent Claims 37 and 44 do not necessarily contain this feature they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

(It is additionally noted that under their present wording Claims 37 and 44 are not unitary with the rest of the subject-matter claimed, as they do not necessarily rely on the inventive concept of employing a polymerase carrying a donor fluorophore in combination with a mixture of nucleotides in which each different type of nucleotide carries a distinguishable acceptor fluorophore).

3. The terms "BODIPY" and "Lissamine" employed in Claims 12 and 18, respectively, and appearing to be registered trade marks, have no precise meaning as they are not internationally accepted as standard descriptive terms, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).
4. The statement in the description on page 32, lines 23-27 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

NOONAN, William
KLARQUIST, SPARKMAN, CAMPBELL,
LEIGH & WINSTON, LLP
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121 S.W. Salmon Street
Portland, Oregon 97204
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing
(day/month/year) 30.10.2001

Applicant's or agent's file reference
4239-55779

IMPORTANT NOTIFICATION

International application No.
PCT/US00/23736

International filing date (day/month/year)
29/08/2000

Priority date (day/month/year)
30/08/1999

Applicant
THE GOVERNMENT OF THE UNITED STATES ...

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Digiusto, M



Tel. +49 89 2399-8162



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4239-55779		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/23736	International filing date (day/month/year) 29/08/2000	Priority date (day/month/year) 30/08/1999	
International Patent Classification (IPC) or national classification and IPC C12Q1/68			
Applicant THE GOVERNMENT OF THE UNITED STATES ...			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the international application 			
Date of submission of the demand 24/03/2001		Date of completion of this report 30.10.2001	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Herrero, M Telephone No. +49 89 2399 8542 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/23736

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-32 as originally filed

Claims, No.:

1-45 as originally filed

Drawings, sheets:

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US00/23736

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 1-45
	No: Claims
Inventive step (IS)	Yes: Claims 1-36, 37-44(part), 45
	No: Claims 37-44 (part)
Industrial applicability (IA)	Yes: Claims 1-45
	No: Claims

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

SECTION V

2. CITATIONS AND EXPLANATIONS

- 2.1 Except for the subject-matter objected to in item 2.2 below (i.e. Claims 37-44, in part) present Claims 1-45 would appear to relate to subject-matter which is novel and non-obvious over the available prior art, as required by Art. 33(2) and (3) PCT. Claims 1-45 also appear to satisfy the requirements of Art. 33(4) PCT.
- 2.2 Under their present wording not all the devices (apparatus) for sequencing a nucleic acid molecule encompassed by independent Claims 37 and 44 comprise, as an essential structural component, a polymerase which includes a donor fluorophore. In particular, in those embodiments encompassed (i) by Claim 37, in which the entity attached to the subject substrate is either an oligonucleotide primer or a sample nucleic acid, and (ii) by Claim 44, in which the entity attached to the glass microscope slide is either an oligonucleotide primer or a sample nucleic acid, a polymerase including a donor fluorophore does not necessarily form part of the claimed devices.

However, the aforementioned devices according to Claims 37 and 44, which do not contain a polymerase including a donor fluorophore as essential constitutive element of the device, would *per se* not be suitable to solve the technical problem of the present invention. As a consequence no inventive contribution over the related prior art would appear to be involved in the provision of such devices, contrary to the requirements of Art. 33(3) PCT.

The same objection (Art. 33(3) PCT) affects *mutatis mutandis* the subject-matter encompassed by dependent Claims 38-43 insofar as a polymerase including a donor fluorophore does not necessarily form part of the corresponding devices therein claimed.

SECTION VII

1. Several terms used in the description appear to be registered trade marks (see e.g. "Triton" or "Tween", on pages 20, 23 and 24), but have not been acknowledged as such.
2. The expression "hereby/herein incorporated by reference" in respect of prior art documents (cf page 10, line 8; page 11, line 23; page 12, lines 9-10, 13 and 38; page 12, line 7; page 18, line 37; page 19, line 7; page 20, lines 3, 19-20, 25-26 and 39; page 22, lines 19 and 22; page 23, line 38; page 24, lines 12, 15 and 18; page 25, line 32; page 26, line 1; page 27, line 9 and page 29, lines 24-25) leads to a doubt as to whether the requirements of the description being self-contained are satisfied (see PCT Guidelines C-II, 4-17).

SECTION VIII

1. It is clear from the description as a whole that the presence of a polymerase carrying a donor fluorophore (e.g. a GFP-polymerase) is a feature essential to the performance of the invention.

Since independent Claims 37 and 44 do not necessarily contain this feature they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

(It is additionally noted that under their present wording independent Claims 37 and 44 are not unitary with the rest of the subject-matter claimed, as they do not necessarily rely on the inventive concept of employing a polymerase carrying a donor fluorophore in combination with a mixture of nucleotides in which each different type of nucleotide carries a distinguishable acceptor fluorophore).

2. The terms "BODIPY" and "Lissamine" employed in Claims 12 and 18, respectively, and appearing to be registered trade marks, have no precise

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US00/23736

meaning as they are not internationally accepted as standard descriptive terms, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT).

3. The statement in the description on page 32, lines 23-27 implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity (Article 6 PCT) when used to interpret them (see also the PCT Guidelines, III-4.3a).

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 4239-55779	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/ 23736	International filing date (day/month/year) 29/08/2000	(Earliest) Priority Date (day/month/year) 30/08/1999
Applicant THE GOVERNMENT OF THE UNITED STATES ...		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.



It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.



the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :



contained in the international application in written form.



filed together with the international application in computer readable form.



furnished subsequently to this Authority in written form.



furnished subsequently to this Authority in computer readable form.



the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.



the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the title,



the text is approved as submitted by the applicant.



the text has been established by this Authority to read as follows:

5. With regard to the abstract,



the text is approved as submitted by the applicant.



the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

as suggested by the applicant.



because the applicant failed to suggest a figure.



because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/23736

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12Q1/68 G01N21/64

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 53805 A (ARMES NIAL ANTONY ;STEMPLE DEREK LYLE (GB); ASM SCIENT INC (US)) 14 September 2000 (2000-09-14) page 19, paragraph 1 ---	1-36
E	WO 00 70073 A (CORNELL RES FOUNDATION INC) 23 November 2000 (2000-11-23) page 38, line 26 -page 39, line 21; figure 1C ---	1-10
A	WO 99 05315 A (DENSAM DANIEL HENRY ;MEDICAL BIOSYSTEMS LTD (GB)) 4 February 1999 (1999-02-04) claims 1-3,22 ---	1-36
A	US 5 707 804 A (JU JINGYUE ET AL) 13 January 1998 (1998-01-13) the whole document --- -/--	1-36

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

29 June 2001

Date of mailing of the international search report

06/07/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Osborne, H

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/23736

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 614 386 A (METZKER MICHAEL L ET AL) 25 March 1997 (1997-03-25) the whole document ----	1-36
A	US 5 674 743 A (ULMER KEVIN M) 7 October 1997 (1997-10-07) cited in the application ----	
A	GORDON GW ET AL: "Quantitative fluorescence resonance energy transfer measurements using fluorescence microscopy" BIOPHYSICAL JOURNAL, vol. 74, May 1998 (1998-05), pages 2702-2713, XP000990953 the whole document -----	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/23736

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0053805	A	14-09-2000	AU 3174600 A	28-09-2000
WO 0070073	A	23-11-2000	AU 5027600 A	05-12-2000
WO 9905315	A	04-02-1999	AU 8455998 A	16-02-1999
			BR 9812270 A	18-07-2000
			CN 1265158 T	30-08-2000
			EP 1017848 A	12-07-2000
US 5707804	A	13-01-1998	US 5654419 A	05-08-1997
			US 6028190 A	22-02-2000
			AU 692230 B	04-06-1998
			AU 1736795 A	21-08-1995
			CA 2182516 A	10-08-1995
			DE 19581489 T	02-01-1997
			DE 29521620 U	13-11-1997
			EP 0743987 A	27-11-1996
			JP 9508525 T	02-09-1997
			WO 9521266 A	10-08-1995
			US 6177247 B	23-01-2001
			US 5688648 A	18-11-1997
			US 5869255 A	09-02-1999
US 5614386	A	25-03-1997	AU 699939 B	17-12-1998
			AU 6288696 A	22-01-1997
			CA 2225531 A	09-01-1997
			EP 0833936 A	08-04-1998
			WO 9700967 A	09-01-1997
			US 5861287 A	19-01-1999
			US 5728529 A	17-03-1998
			US 5994063 A	30-11-1999
US 5674743	A	07-10-1997	AU 1228197 A	27-03-1997
			AU 673245 B	31-10-1996
			AU 6131694 A	29-08-1994
			CA 2155186 A	18-08-1994
			EP 0682671 A	22-11-1995
			JP 8506664 T	16-07-1996
			MX 9400837 A	31-08-1994
			WO 9418218 A	18-08-1994

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 March 2001 (08.03.2001)

PCT

(10) International Publication Number
WO 01/16375 A2

- (51) International Patent Classification⁷: **C12Q 1/68**, (74) Agent: NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Winston, LLP, Suite 1600, One World Trade Center, 121 SW Salmon Street, Portland, OR 97204 (US).
G01N 21/64
- (21) International Application Number: PCT/US00/23736
- (22) International Filing Date: 29 August 2000 (29.08.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
60/151,580 30 August 1999 (30.08.1999) US
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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— Without international search report and to be republished upon receipt of that report.
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HIGH SPEED PARALLEL MOLECULAR NUCLEIC ACID SEQUENCING

(57) Abstract: A method and device is disclosed for high speed, automated sequencing of nucleic acid molecules. A nucleic acid molecule to be sequenced is exposed to a polymerase in the presence of nucleotides which are to be incorporated into a complementary nucleic acid strand. The polymerase carries a donor fluorophore, and each type of nucleotide (e.g. A, T/U, C and G) carries a distinguishable acceptor fluorophore characteristic of the particular type of nucleotide. As the polymerase incorporates individual nucleic acid molecules into a complementary strand, a laser continuously irradiates the donor fluorophore, at a wavelength that causes it to emit an emission signal (but the laser wavelength does not stimulate the acceptor fluorophore). In particular embodiments, no laser is needed if the donor fluorophore is a luminescent molecule or is stimulated by one. The emission signal from the polymerase is capable of stimulating any of the donor fluorophores (but not acceptor fluorophores), so that as a nucleotide is added by the polymerase, the acceptor fluorophore emits a signal associated with the type of nucleotide added to the complementary strand. The series of emission signals from the acceptor fluorophores is detected, and correlated with a sequence of nucleotides that correspond to the sequence of emission signals.

WO 01/16375 A2

(12) INTERNATIONAL PUBLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
8 March 2001 (08.03.2001)

PCT

(10) International Publication Number
WO 01/16375 A3

- (51) International Patent Classification⁷: C12Q 1/68, G01N 21/64
- (21) International Application Number: PCT/US00/23736
- (22) International Filing Date: 29 August 2000 (29.08.2000)
- (25) Filing Language: English
- (26) Publication Language: English
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- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:
— with international search report
- (88) Date of publication of the international search report:
4 October 2001
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



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WO 01/16375 A3

PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 04 May 2001 (04.05.01)	Applicant's or agent's file reference 4239-55779
International application No. PCT/US00/23736	Priority date (day/month/year) 30 August 1999 (30.08.99)
International filing date (day/month/year) 29 August 2000 (29.08.00)	
Applicant SCHNEIDER, Thomas, D. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

24 March 2001 (24.03.01)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Zakaria EL KHODARY Telephone No.: (41-22) 338.83.38
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